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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,161	01/19/2001	Michael S. Colman	MCA-538	9144

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EXAMINER	
MENON, KRISHNAN S	
ART UNIT	PAPER NUMBER
1723	13

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,161	COLMAN, MICHAEL S.	
	Examiner	Art Unit	
	Krishnan S Menon	1723	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *RCE/amendment of 2/26/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-19 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 14-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not support the elements " ... providing an ultrafiltration membrane having a characterized molecular weight limit.." and "..nucleic acids having... molecular weight below said characterized...". The specification as originally filed does not seem to support a method of filtering nucleic acids of molecular weights lower than the 'characterized molecular weight limit' of the membrane.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bussey et al (US 6,011,148).

Claims 17-19: Bussey teaches a process of ultrafiltration of nucleic acids (abstract, col 5 lines 3-6), using differential pressure as a driving force (col 7 lines 30-45), from a liquid sample by diluting the sample (col 7 lines 44-55) in order to retain pure nucleic acids as in claim 17. The diluent comprises water, Tris-HCl, EDTA etc as in claim 19 (col 11 lines 50-65, col 10 lines 5-15).

Bussey does not teach fractionation of DNA fragments, and expresses the retention of the nucleic acids in terms of molecular weights instead of base pairs as in claims 17 and 18. The instant application only describes the process of purifying DNA fragments using ultrafiltration with increased recovery by dilution of the sample, even though the application recites the process as "fractionation" (see page 2 para 2 and 3, page 3 para 1 and 2, last 2 lines of page 4, para 3 of page 6, etc.). Bussey uses the same method of dilution, similar ultrafiltration membranes (compare the membrane – col 6 lines 24-54), and the same differential pressure as in the instant application, and therefore, it would be obvious to one of ordinary skill in the art at the time of invention that the process taught by Bussey also would provide the same recovery of the nucleic acid fragments as in the instant application.

Claims 14-16: Claim 17 recites all the limitations of claim 14 as above, except, the nucleic acids are characterized by case pairs instead of molecular weights. Bussey teaches the process of "fractionation" of nucleic acids on the basis of molecular weight using membranes of characterized molecular weight limits (col 6 lines 24-53). Bussey does not specifically teach that the membranes would retain nucleic acid fragments by dilution of the samples which otherwise would pass through. However, it would be obvious to one of ordinary skill in the art at the time of invention that since Bussey uses the same method of dilution, and the same differential pressure as in the instant application, and therefore, the process taught by Bussey also would provide the same recovery of the nucleic acid fragments as in the instant application.

Claims 15 and 16 add further limitations of degree of dilution (col 7 lines 44-54) and constant pressure (col 7 lines 29-44).

2. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bussey (148) in view of WO 00/66723).

Claim 1: Bussey teaches a process of ultrafiltration of nucleic acids (abstract, col 5 lines 3-6), using differential pressure as a driving force (col 7 lines 30-45), from a liquid sample by diluting the sample (col 7 lines 44-55) in order to retain pure nucleic acids as in claim 17. Bussey does not teach fractionation, fragment length, and diluting to dryness. The instant application only describes the process of purifying DNA fragments using ultrafiltration with increased recovery by dilution of the sample, even though the application recites the process as "fractionation" (see page 2 para 2 and 3, page 3 para 1 and 2, last 2 lines of page 4, para 3 of page 6, etc.). Bussey uses the same method of dilution, the same differential pressure as in the instant application, and similar ultrafiltration membrane, and therefore, it would be obvious to one of ordinary skill in the art at the time of

invention that the process taught by Bussey also would provide the same recovery of the nucleic acid fragments as in the instant application. Re filtration to dryness, WO-723 teaches ultrafiltration to dryness of nucleic acid samples with membranes. It would be obvious to one of ordinary skill in the art at the time of invention to use the teaching of WO-723 in the teaching of Bussey to filter the sample to dryness to handle multiple samples in one step with multi-well filters (see WO 723 abstract).

Claim 2: The dilution is encompassed (col 7 lines 44-55) of Bussey's teachings of diafiltration and continuous diafiltration.

Claim 3: Bussey teaches the diluents water, EDTA , Tris-HCl, and their mixtures (lines 5-20 of col 10, and lines 45-55 of col 11.)

Claim 4: Teaches separating the double stranded DNA or RNA (col 3, lines 24-32), when he states that the concentration of the single stranded DNA is less than 1%.

Claim 5: the pressure differential (trans-membrane pressure) is constant (Lines 28-32, col. 7)

Claim 6, 7 and 8 adds further limitations over claim 1: In addition to the recovery of nucleic acids with ultrafiltration membranes at constant pressure differential (see above), the pressures 25" Hg and 10" Hg fall within the range taught by Bussey. The ultrafiltration membrane has upstream (feed) and downstream (permeate) sides (col 7 lines 25-45).

3. Claims 9-12 rejected under 35 U.S.C. 103(a) as being unpatentable over Bussey (148) in view of Simon (us 5,434,048).

Bussey (148) discloses a process for "fractionation" of contaminants by adding to said sample monovalent cations (col 10, lines 5-20) and contacting said sample with an ultrafiltration membrane and subjecting a pressure differential to the sample as discussed above. Bussey does not

teach the use of condensing agents like bivalent cations as recited by claims 9 and 10. Simon (048) teaches the use of monovalent and bivalent cations, i.e., KCl and MgCl2 (examples I and II) for removal of contaminants by ultrafiltration (col 3 lines 14-17). It would be obvious to one ordinarily skilled in the art at the time of invention to use Simon's teachings of using bivalent cations with Bussey's teachings of removal of contaminants from the sample using an ultrafiltration membrane under a pressure differential for asymmetric amplification as taught by Simon (col 4 lines14-17).

Claims 11 and 12 add further limitations of monovalent cations (claim 11) and constant pressure differential (claim 12) (see Bussey: example I; col 7 lines 29-44)

4. Claim13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bussey.

While Bussey teaches all the limitations of claim 13, as explained in the forgoing paragraphs. Bussey does not specifically state the use of a first and then a second pressure. However, Bussey teaches that "Generally filtration process is faster with higher pressures, but higher pressures are likely to cause shearing of the nucleic acid or loss due to passage through the membrane" (lines 30-40, col 7). Therefore, it is obvious for one of ordinary skill in the art at the time of the invention that flow of DNA fragments through an ultrafiltration membrane is pressure dependent and one could subject the samples to different pressures to obtain different flow rates of each species. It is also obvious to one ordinarily skilled in the art at the time of invention that filtering a second time with a different pressure would result in better recovery as taught by Bussey, because lower trans-membrane pressures would afford recovery of lower nucleic acid fragments (col 7 lines 30-40).

Response to Arguments

Re claim 14, applicant argues that, although there is no express support to language that is objected to, it is well known .. that ultrafiltration membrane has a molecular weight limit. In the examiner's knowledge, while this statement is true as a general thumb rule, it is not very precise. Molecular weight cut off of ultrafiltration membranes are determined (or characterized) by using globular macromolecules (like dextran) of precisely determined molecular weights (see Busy '148 col 4 lines 44-55). In the instant application, the applicant recites a method in which recovery of smaller fragments of nucleic acids is improved by diluting the sample to increase the fragment length when filtering using a commercial off the shelf ultrafiltration membrane. The molecular weight limit of the membrane with respect to the molecular weight of nucleic acids, whether predetermined or characterized, is not originally described in the specification.

Rest of the arguments, directed at the Schneider reference, are moot because of the new grounds for rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Krishnan S Menon whose telephone number is 703-305-5999. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Wanda L Walker can be reached on 703-308-0457. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9310 for regular communications and 703-872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Krishnan Menon
Patent Examiner
April 3, 2003

JOSEPH DRODGE
PRIMARY EXAMINER